عنوان مقاله:

Underlying anti-cancer mechanisms of histone deacetylase (HDAC) inhibitors in tamoxifen-resistant breast cancer cells

محل انتشار:

مجله علوم پایه پزشکی ایران, دوره 27, شماره 6 (سال: 1403)

تعداد صفحات اصل مقاله: 5

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خلاصه مقاله:

Objective(s): Breast cancer is an important women's malignancy with high cancer-related deaths worldwide. Drug resistance lowers the treatment efficacy in this malignancy. This study aimed to explore the underlying mechanisms of histone deacetylase (HDAC) inhibitor trichostatin A (TSA) to overcome resistance to tamoxifen in breast cancer cells.Materials and Methods: Tamoxifen-resistance in MCF-۷ breast cancer cells was simulated. MTT assay was used to detect the cytotoxic effects of HDAC inhibitor and PI۳K inhibitor on the cancer cells. Trans-well assay was applied to evaluate the invasion and migration of the treated cancer cells. Flow cytometer assay was also applied to evaluate cell cycle phases in the treated cancer cells. Finally, expression of vascular endothelial growth factor (VEGF), E-cadherin, Vimentin, phosphorylated phosphatidylinositol kinase (p-PI۳k), phosphorylated protein kinase B (p-AKT), and phosphorylated mammalian target protein of rapamycin (p-mTOR) was evaluated by western blotting.Results: The obtained results indicated that HDAC inhibitor treatments significantly decreased viability, migration, and invasion in the cancer cells. Furthermore, the frequency of the treated cancer cells significantly increased in the S phase as well as significantly decreasing in the G۲/M phase of the cell cycle. Moreover, HDAC inhibitor modified levels of VEGF, E-cadherin, Vimentin, p-PI۳k, p-AKT, and p-mTOR proteins. However, HDAC inhibitor combined with PI۳K inhibitor exerts more profound effects on the cancer cells as compared to HDAC inhibitor monotherapy.Conclusion: HDAC inhibitors inhibited the survival of breast cancer drug-resistant cells, invasion, migration, and angiogenesis by inhibiting the PI۳k/Akt/mTOR signaling pathway.

کلمات کلیدی:

Anti-cancer, Breast Cancer, Drug resistance, Histone deacetylase- inhibitors, Tamoxifen

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